Analysis of the Inverse Association between Cancer and Alzheimer's Disease: Results from the Alzheimer's Disease Neuroimaging Initiative Cohort

Kelly N.H. Nudelman, Shannon L. Risacher, John D. West, Kwangsik Nho, Vijay K. Ramanan, Brenna C. McDonald, Li Shen, Tatiana M. Foroud, Bryan P. Schneider, Andrew J. Saykin

Abstract

Although a number of studies support a reciprocal inverse association between diagnoses of cancer and Alzheimer's disease (AD), to date there has not been any systemic investigation of the neurobiological impact of or genetic risk factors underlying this effect. To facilitate this goal, this study aimed to replicate the inverse association of cancer and AD using data from the NIA Alzheimer's Disease Neuroimaging Initiative, which includes age-matched cases and controls with information on cancer history, AD progression, neuroimaging, and genomic data. Subjects included individuals with AD (n=234), mild cognitive impairment (MCI, n=542), and healthy controls (HC, n=293). After controlling for sex, education, race/ethnicity, smoking, and apolipoprotein E (*APOE*) e2/3/4 allele groups, cancer history was protective against baseline AD diagnosis (p=0.042), and was associated with later age of AD onset (p=0.001). Cancer history appears to result in a cumulative protective effect; individuals with more than one cancer had a later age of AD onset compared to those with only one cancer (p=0.001). Finally, a protective effect of AD was also observed in individuals who developed incident cancer after enrolling (post-baseline visit); 20 individuals with MCI and 9 HC developed cancer, while no AD patients had subsequent cancer diagnoses (p=0.013). This supports previous research on the inverse association of cancer and AD, and importantly provides novel evidence that this effect appears to be independent of *APOE*, the major known genetic risk factor for AD. Future analyses will investigate the neurobiological and genetic basis of this effect.

244 / 250 words